Appl Health Econ Health Policy
https://doi.org/10.1007/s40258-018-0374-x

COMMENTARY

Medicinal Cannabis and the Tyranny of Distance: Policy Reform Required for Optimizing Patient and Health System Net Benefit in Australia

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In the evolution of any novel concept, there is a spectrum in the rate at which individuals adopt a new idea, a diffusion of innovation stretching from innovators to laggards [1]. Such a distribution is emerging globally in the rapidly evolving field of medicinal cannabis (MC). Countries such as Israel, the Netherlands and, more recently, Canada could be regarded as innovators [2, 3]. They have taken pragmatic health system-based responses to the needs of patients, facilitating access to those with highest expected net clinical benefit while conducting trials and studies in parallel. Even the USA, with its patchwork quilt of innovation and lack of federal oversight, is developing insights into what works for their patient populations, and what doesn't [4].

In contrast, Australia cannot be regarded as an innovator while obstacles continue to thwart the creation of an efficient, patient-oriented system, despite intentions of Federal legislation passed in February 2016 [5]. Obstacles thrown up are at least evolving, from dated questions such as the validity of using botanical products to treat medical conditions, to allegations that those same products cannot be dosed appropriately. Yet reasons for denying access continue to confound recreational and medicinal cannabis, either deliberately or through ignorance. The suggestion that a medicinal cannabis compassionate access scheme risks being diverted into the hands of recreational consumers should be treated with derision in a country where recreational cannabis is already easily obtainable and medicinal cannabis is grown and produced for therapeutic rather than psychotropic effects.

The lack of health system access in general is not a consequence of there being negative research findings, but rather a concerted attempt over most of the last century to prevent and stifle research into therapeutic effects [6]. To further elucidate and optimise the potential of medicinal cannabis across all symptoms related to the body's endocannabinoid system in enabling organ system homeostasis, there is no doubt that further research is needed. However, there is also no doubt that there are prevalent compassionate access patient populations in Australia that can gain substantial net clinical benefit and health systems net benefit right now as in other countries in practice as well as in trial settings [7, 8], given synthesis of current international knowledge and evidence [2–4, 7–15].

1 Synthesising International Scientific, Trial and Practice Evidence

So what is the evidence that has arisen in the lands of innovators, free from the tyranny of distance? In February 2017, in the most comprehensive international review to date, the US National Academy of Science (NAS) report [4] found definitive highest tier evidence of MC effectiveness in adult populations with:

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Journal : Large 40258 | Dispatch : 22-2-2018 | Pages : 4
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MS Code : AHEA-D-17-00211 | ☑ CP | ☑ DISK

1. Chronic pain (by far the most prevalent population for MC use internationally, e.g. 90% of 1.02 million registered MC users in the USA, 70% as a primary symptom [3]);
2. Antiemetic treatment in patients undergoing chemotherapy; and
3. Multiple sclerosis populations, for spasticity.

The NAS review also highlighted the need for public health and health economic evidence synthesis in informing optimal policy responses.

The response of the Australian Government was to announce a 'review of reviews', with tremendous reluctance to include 'non-cancer pain' in the range of indications reviewed. This lack of consideration and potential for appropriate access is particularly concerning given the very real current endemic problems of long-term opiate use for chronic pain, particularly chronic neuropathic pain. Aside from trial evidence, MC use for pain populations is supported by compelling population evidence of MC programs acting as an exit drug in reducing opioid-related deaths, on average by 24.8% across 13 US states with MC programs between 1999 and 2010, and increasing to 33% by 6 years [9]. Furthermore, Bradford and Bradford show reduction in pain prescription medication use by 12 and 8–13% for other major prescription medications for anxiety, depression, nausea, psychosis and sleep disorder [10].

Importantly, scientific and trial research evidence has found a synergistic phenomenon—referred to as the 'entourage effect' within the field—between terpenes and cannabinoids (cannabidiol (CBD), tetrahydrocannabinol (THC) and potentially other minor cannabinoids), which both magnifies therapeutic impacts and minimises side effects [11, 12]. For example, in chronic and intractable palliative and cancer pain populations, the most comprehensive three-arm RCT compared terpene-rich THC and CBD (1:1), THC and opioids alone. In the terpene-rich arm 43% had significant (greater than 30%) pain reduction response, compared with 21% for opioids and 23% for THC alone [12].

Critically, these clear 'entourage' benefits imply that pharmaceutical company processing of MC to a narrow, single-agent spectrum of action will not maximise net clinical nor economic benefits from medicinal cannabis. Rather, they support whole plant products or extracts on both clinical and economic grounds. Several internationally renowned companies, in particular Tikun Olam (Israel) and Bedrocan BV (Netherlands), distribute whole plant cultivars and extracts appropriate to indications, with extensive experience in maximising symptom relief and net clinical benefit for MC patients. Their palette of terpene-, CBD- and THC-rich cultivars and extracts are already securely produced with Good Agricultural Practice (GAP) and using Good Manufacturing Practice (GMP). Dosing is individualised and titrated, in the same way it is for gabapentin [13], with the process codified in Israel in 'The Green Book', a prescribing manual for clinicians [14].

Australia is climatically well-suited to the cultivation of higher quality CBD-, THC- and terpene-rich medicinal cannabis varieties, which grow better in the types of microclimates that Australia has in abundance, with appropriate latitudes, natural sunlight, air and space. Alongside better-quality MC for symptom relief, outdoor and greenhouse cultivation with these varieties enables both direct therapy and downstream cost savings compared to indoors. In terms of direct costs, greenhouse and outdoor cultivation in natural sunlight are estimated with RAND analysis to respectively be 40% and 10% the cost of indoor cultivation [15]. In Australia, this would equate to expected distributed therapy cost savings per patient treated of A$10 a day or A$3650 per year for appropriate highest quality GAP and GMP varieties grown outdoors, compared to growing these varieties indoors, or relative to 'value-based' pricing of current pain management therapies [3, 8]. Distributed therapy cost of appropriate highest quality GMP and GAP domestically cultivated MC varieties (outdoors $A1–1.25 for average dose of 1 gram per day vs $A10–12.50 indoors, with cultivation 20% of this cost [15]) reflect factor pricing with normal profits. Imported 'value based' pricing relative to current opioid based therapies is estimated as $A11 per day, or higher with greater effect for MC therapies where patented (synthetic) [3, 8], reflecting super normal profits in appropriating all consumer surplus [8, pp. 255–278; 16, 17].

Consequently, at a population level appropriate health shadow pricing reflecting the true opportunity cost [8, 16, 17] of optimal outdoor grown domestic terpene rich MC plant based therapy leads to expected direct therapy cost savings in Australia of A$730 million or more annually in a population of 200,000 [8, pp. 299–301]. Trial evidence in intractable pain populations [12] also points to downstream hospital cost savings in patients with better pain relief relative to current opioid therapies (43 vs. 21% $p = 0.014$). Furthermore, in palliative populations, alongside better symptom control, such quality-assured MC is immune-supportive and enables better meeting key palliative care domains compared to alternative therapies [18, 19] in finalising personal affairs with whom they want to be with (family and friends) and in their community of choice (usually at home) without the need for institutional care.

Such health benefits and health system cost savings are expected to grow commensurate with 'baby boomer' generation needs for palliative and chronic pain management aiding their successful ageing and health budgets alike [8].

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While Australia continues to sit on the fence, the MC market globally is projected to increase almost fivefold from $USD11.4 billion to US$55.8 billion by 2025 [2]. Perhaps this explains why the government is so interested in exploring export options prior to ensuring appropriate domestic access [20].

2 Why is Medicinal Cannabis Not Currently Accessible in Australia Given Expected Patient and Health System Net Benefit?

An argument has been made in Australia that if cannabis is to be considered as a medicine, it must be considered as a 'new drug' rather than as a plant. Australia remains the only First World country to attempt this, and without the benefit of a specific MC Regulator. A Bill for such a regulator was put to committee in 2014, with bipartisan support [21], only to be withdrawn on the insistence that standing regulatory mechanisms overseen by the Office of Drug Control (ODC) and the Therapeutic Goods Administration (TGA) would suffice. The success, or rather lack thereof, of this approach as far as access and net benefit to patient and the health system is now evident. In the absence of true federal leadership, states and territories are developing their own approaches, as has happened in the USA, in an effort to facilitate patient access. An unintended consequence for patients and prescribers has been to now find themselves facing two tiers of regulations to navigate, of which the federal level is likely to change at short notice. The removal of MC from Special Access Scheme Category A—without patient or prescriber consultation—and its subsequent reinstatement as a consequence of the ensuing public outcry [22], is an example of the vagaries facing patients.

What lies beneath this apparent conservatism? One must ask Cicero's question: "Qui bono?"—"Who stands to gain"? It is reasonable that Australia, as a significant global grower of opium poppy straw in Tasmania, might see advantage in treading cautiously, to guarantee compliance with the International Drug Treaties. However, the main party with an interest in this space is the pharmaceutical industry. In an era where the misdemeanors of the industry, particularly in opiate provision, are now not only a matter of common knowledge, but also the cause of a global public health crisis, any entity that might encroach on the market share for analgesia might be considered an economic competitor. The extent to which Pharma is inveigling itself in the anti-MC movement in the USA is only just becoming apparent, from funding electoral ballot positions [23] to subsidising vocal anti-MC clinicians [24].

3 Conclusion

As Australia contemplates 'baby boomer' ageing, it can benefit from reflecting on how the wider world is addressing medicinal cannabis. The rest of the world has not held its collective breath for trial results from Australia before pressing on with patient treatment. In the age of the Internet, immediate communication and a global economy, it is no longer a tenable option for opponents of MC to hope that Australian patients might somehow opt for a less compassionate approach to care than those of their overseas counterparts. A middle ground exists between those who believe that MC is a panacea for all ills, and those that believe that there is no role for MC for anyone; our ability to navigate the path between the two will be judged by history. If we are not compassionate and clever, brave and kind, history is unlikely to be kind with us.

Compliance with Ethical Standards

This commentary received no financial funding.
David Caldicott, Justin Sinclair, Lynnaire Sheridan and Simon Eckermann have no conflicts of interest. David Caldicott is a member of the ACT Medical Cannabis Advisory Group. Justin Sinclair, David Caldicott and Simon Eckermann are members on the Scientific Board of United in Compassion. Justin Sinclair is a member of the Scientific Advisory Board of BioCeuticals.

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